

## REMARKS

### I. Status of Claims

Claims 1 - 19 are canceled.

Claims 22 – 39 are withdrawn.

Claims 20 and 21 are amended.

Claims 40 – 44 are added.

Claims 20 – 21 and 40 – 44 are pending.

### II. Support for Claim Amendments

Elected Group I was said by the examiner to include claims 16-21 to an “isolated zebrafish,” but claims 20 and 21 originally referred to a “fish model.” Therefore, claims 16-18 are cancelled, and claims 20-21 are amended to relate modeling.

Further support for a method to compare effects of genetic mutations of zebrafish to characteristics of mammalian dystrophic conditions, e.g. human forms of muscular dystrophy/cardiopathy, to delve into genetic mechanisms, are in the specification in at least the following locations (citations are to US 2007/0056054 A1) [0008], [0012], [0013], [0023-0027].

New claims 40 to 44 based on cancelled claims 17 to 19.

### III. Granato Does Not Have All Claim Elements so Cannot Anticipate

Claims 16 – 21 were rejected under 35 U.S.C. §102(b) by Granato.

There is no teaching or suggestion by Granato *et al.* that *sapje* zebrafish mutants could be used as a model for muscular dystrophy. Accordingly, it is submitted that claims are novel and involve an inventive step.

Granato *et al* 1996 looked at 166 mutants in zebrafish with primary locomotion defects. A number of A4 mutants including *sapje* (*sap*) with reduced striation and somite degeneration were identified and their significance is discussed on page 403, second column, and page 409, second column. Granato *et al* identified that the *sapje* zebrafish mutants have muscle degeneration. However, they did not identify a particular muscular dystrophy disease, or the mutation within the gene

causing the muscle degeneration, within the sapje zebrafish. The underlying basis for the present invention is the discovery that the muscle wasting pathology evident in the sapje strains results from a mutation in the zebrafish dystrophin gene, and thus use and application in screening for therapeutic intervention in human muscular dystrophy is novel.

Muscular dystrophy is the name given to a group of nine different diseases characterized by skeletal muscle degeneration. These diseases are Becker, Congenital, Duchenne, Distal, Emery-Dreifuss, Facioscapulohumeral, Limb-Girdle, Myotonic and Oculopharyngeal muscular dystrophy. Each of these diseases has a different etiology and presentation. In addition, there are over 100 different diseases which have similarities to muscular dystrophy. A model for muscular dystrophy in humans will be very useful in the study of the disease. Furthermore, having a model able to differentiate muscular dystrophy from other neuromuscular diseases is valuable in the investigation and development of treatments for muscular dystrophy.

The present disclosure identifies the *sapje* zebrafish mutant is caused by a mutation within the zebrafish dystrophin gene. The inventors confirmed that the zebrafish dystrophin gene corresponds to the human dystrophin gene by sequence analysis and using antibodies raised against mammalian dystrophin. Genetic lesions within the human dystrophin gene lead to the onset of Duchenne and Becker muscular dystrophies. The inventors established that the *sapje* zebrafish exhibit muscle degeneration is reminiscent of human Duchenne and Becker muscular dystrophies and therefore can be used as a model of muscular dystrophy, particularly the human disease.

An anticipating prior art reference should disclose each and every limitation of the claim expressly or inherently. *Akamai Techs. v. Cable & Wireless Internet Servs.*, 344 F.3d 1186, 1192 (Fed. Cir., 2003). To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996). To serve as an anticipating reference, a reference must enable that which it is asserted to anticipate. *Elan Pharms., Inc. v. Mayo Found.*, 346 F.3d 1051, 1054 (Fed. Cir., 2003). The dispositive question regarding anticipation is whether one skilled in the art would reasonably understand or infer from the prior art reference's teaching that every claim limitation was disclosed in that single reference. *Dayco Prods., Inc. v. Total*

*Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003) (internal quotation marks and alterations omitted).

Granato does not teach a model relating the zebrafish mutants to the dystrophin gene, and to human dystrophic conditions, e.g., muscular dystrophy/cardiomyopathy. Therefore, Granato does not anticipate. Please withdraw this rejection.

#### **IV. Other Issues**

Embedded hyperlinks from the specification have been removed by amendments.

A copy of an executed Declaration from Peter Currie is enclosed to meet the formality issue.

Applicants request allowance of the pending claims. No other fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (36180-100472).

Respectfully submitted,



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